REMARKS

Claims 1-48 are currently pending in the instant application. The present Office Action includes rejections under 35 U.S.C. §102 and §103, responses to which are discussed below.

Applicants have replaced pending claims 1-48 with new claims 49-87. By way of assistance, the chart on the following page shows any corresponding old claim(s) that may substantially correlate to the new claims. The chart also shows the old claims that were alleged to be anticipated by Nguyen (U.S. Pat. No. 5,843,347) or Rambert (Neuropharmacology, 1994) in the first office action.

New Claim No.	Old Claim No.	§102: Nguyen	§102: Rambert
49	1, 2, 3	1, 3	yes
50	7		
51	5	yes	yes
52	4	yes	yes
53	new		
54	6		
55	new		
56	8		
57	9		
58	13-15, 18	13, 15, 18	yes
59	21		yes
60	22		
61	new		
62	23		
63	35	yes	yes
64	38	yes	yes
65	37, 40		yes
66	new		
67	17	yes	yes
68	new		
69	46	yes	yes
70	47		
71	48	yes	yes
72	19	yes	yes
73	28		yes
74	45		
75	20	yes	
76	44		
77	24	yes	yes
78	25		yes
79	26		
80	27		
81	41-43, new	41, 42	yes
82	45		
83	29-30	yes	
84	31	yes	
85	32		
86	33		
87	34		

No new subject matter has been added. All of the amendments are supported by the specification, details of which are provided below.

New independent claim 49 combines old claims 1, 2, and 3. New claim 53 claims the levorotatory form of modafinil, support for which can be found on page 1, lines 26-29. Support for new claim 55 can be found on page 10, line 24, and in Example 1, page 16, lines 22-29.

New independent claim 58 combines old claims 13-15 and 18. Support for new claim 61 can be found on page 10, line 24, and in Example 1, page 16, lines 22-29. New claim 66 finds support on page 9, lines 31 through page 10, line 6. New claim 68 claims the levorotatory form of modafinil, support for which can be found on page 1, lines 26-29.

New independent claim 83 combines old claims 29 and 30.

Rejection under 35 U.S.C. §102(b)

Claims 1, 3-5, 10-13, 15-20, 24, 29-31, 35, 36, 38, 39, 41, 42, 46, and 48 are rejected under 35 U.S.C. §102(b) as being anticipated by Nguyen with Hedges to support inherency.

Applicants have submitted new independent claim 49, and the corresponding dependent claims 50-57, which incorporate the limitations of old claim 2, that is, an inclusion complex wherein the modafinil compound has an aqueous solubility of at least 10 mg/ml. Old claim 2 was not subject to the §102(b) rejection over Nguyen. Hence Applicants submit that new claims 49-57 drawn to inclusion complexes wherein the modafinil compound has an aqueous solubility of at least 10 mg/ml are novel with respect to Nguyen.

Similarly, Applicants have submitted new claim 58, and the corresponding dependent

claim 59-82, which incorporate the limitations of old claim 14, that is, a pharmaceutical composition wherein the modafinil compound has an aqueous solubility of at least 10 mg/ml. Old claim 14 was not subject to the §102(b) rejection over Nguyen. Hence Applicants submit that new claims 49-57 drawn to inclusion complexes wherein the modafinil compound has an aqueous solubility of at least 10 mg/ml are novel with respect to Nguyen.

Similarly, Applicants submit that new claims 83 and 84 which also include the limitation that the modafinil compound has an aqueous solubility of at least 10 mg/ml are novel with respect to Nguyen. New claim 85-87 substantially correspond to old claims 32-34, which were not subject to the §102(b) rejection over Nguyen et al

In view of the above amendments and remarks, reconsideration and withdrawal of the rejection under §102 is respectfully requested.

Claims 1-5, 9, 10, 12-19, 21, 24, 25, 28, 35-43, 46, and 48 are rejected under 35 U.S.C. §102(b) as being anticipated by Rambert with Hedges to support inherency. It is asserted in the Office Action that Rambert exemplifies modafinil solubilization corresponding to 10 mg/ml and 20 mg/ml. It is respectfully submitted that these teachings are incorrect, as discussed below.

In this regard, Applicants submit, pursuant to 37 CFR 1.132, the Declaration of Dr. Martin Jacobs (hereinafter "the Declaration"), an inventor in the present application. The Declaration establishes that the solutions taught in Rambert did not fully solubilize modafinil at 10 mg/ml or higher.

Dr. Jacobs is an expert in the field of pharmaceutical formulations, particularly as it relates to formulations of modafinil. He states in the Declaration that experiments were conducted to test the solubilization of modafinil under the conditions presented in Rambert

(Declaration, ¶ 7-8). The Rambert publication teaches aqueous solubilization of a mixture of 100 μg of modafinil in 10 μL of 1% hydroxy-propyl-betacyclodextrin solution, which is equivalent to 10 mg/ml, and a 200 μg of modafinil in 10 μL of 2% hydroxy-propyl-betacyclodextrin solution, which is equivalent to 20 mg/ml (Declaration, ¶ 7).

The Declaration establishes that it was not possible to prepare a fully solubilized 10 mg/ml solution of modafinil in a 2% hydroxy-propyl-betacyclodextrin solution (by weight) at room temperature (Declaration, ¶ 8). The Declaration further establishes that the degree of solubilization of modafinil in a 2% solution of 2-hydroxypropyl-β-cyclodextrin was less than 5 mg/ml (Declaration, ¶ 8, 12).

New claims 49-87 incorporate the limitation that the modafinil compound has an aqueous solubility of at least 10 mg/ml. As stated by Dr. Jacobs, the claims with this limitation are distinguishable over the teachings of Rambert (Declaration, ¶ 13).

In view of the foregoing discussion and enclosed Declaration, reconsideration and withdrawal of the rejection under §102 is respectfully requested.

Rejection under 35 U.S.C. §103(a)

Claims 1-5, 9-21, 24, 29-31, 35, 36, 38, 39, 41, 42, 46, and 48 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nguyen. The Office Action alleges that while the reference does not exemplify the full range of cyclodextrins, it would have been obvious to one skilled in the art to use any of the cyclodextrins suggested by the reference and that one of ordinary skill would expect success in making this modification.

Applicants respectfully submit that Nguyen fails to teach the claimed invention. The instant claims involve the formation of inclusion complexes of a modafinil compound and a cyclodextrin such that modafinil has an aqueous solubility of at least 10 mg/ml. Nguyen

teaches mechanical processes of extruding and lyophilizing a "pasty mixture" within a defined viscosity range (see col. 5, lines 8-9) for the preparation of matrix particles (col 3, lines 30-43). The teachings are directed to the composition of this "pasty mass" which comprises two essential components: (b1) a polymer, and (b2) a water soluble component (col. 5, line 65 to col. 6, line 5). Component (b2) is acts as physiologically inert diluent or ballast and is used for cohesion of the microparticles (see col. 6, lines 32-35). Nguyen teaches component (b2) can be selected from lactose, glycocoll, mannitol, glucose, sucrose, maltodextrin, and artificial sweeteners such as aspartame, cyclamates and saccharinates, along with cyclodextrins (col. 6, lines 44-49).

Applicants respectfully submit Nguyen fails disclose the formation of a modafinil/cyclodextrin inclusion complex, nor does it disclose that such a complex solubilizes modafinil in water, nor does it disclose an aqueous solubilization of modafinil of 10 mg/ml.

Furthermore, there is little suggestion to one skilled in the art to modify the teachings of Nguyen to arrive at the instant invention, nor that such modifications would succeed. One skilled in the art would be hard pressed to make modifications to a teaching that is directed to a mechanical process for lyophilization and extrusion of a pasty mixture, where the components that comprise the pasty mixture are selected to facilitate ease in extrusion of the pasty mixture through an extrusion head, and where the extrudate is subsequently lyophilized. One of the components of the pasty mixture is selected to act as a water-soluble diluent, and consists of 10 classes of sugar derivatives and artificial sweeteners, one of which is a cyclodextrin. In other words, the teachings suggest use of the cyclodextrin as a sugar derivative, not as a complexing agent. There is no suggestion that cyclodextrin was used to form an inclusion complex with the active agent, nor that inclusion complexes with the active

were even formed, nor were there any other complexing agents taught in the reference.

Hence, Nguyen fails to teach the disclosure of the instant application, nor does it provide one skilled in the art with any incentive to modify the teachings of Nguyen in such a manner as to arrive at the instant invention, nor is there a suggestion that any such modifications would succeed. As such, Applicants respectfully submit the new claims are non-obvious over Nguyen et al and request that the rejection be withdrawn.

Claims 25-27, 32-34, 44, and 45 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nguyen et al in view of Grebow. The Office Action alleges that it would be obvious to one skilled in the art to use the Nguyen composition for the treatment of the disorders disclosed in Grebow.

Applicants respectfully submit that Grebow does not cure the deficiencies of Nguyen that were discussed previously and that the instant claims are non-obvious over Nguyen et al in view of Grebow. Hence, the new claims have not been taught nor suggested by the references, alone or in combination, and as such are non-obvious.

Claims 32-34 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nguyen et al in view of Lafon, Scammel, or Miller. The Office Action alleges that it would be obvious to one skilled in the art to use the Nguyen composition for the treatment of the disorders disclosed in Lafon, Scammel, and Miller.

Applicants respectfully submit that Lafon, Scammel, or Miller do not cure the deficiencies of Nguyen that were discussed previously and that the instant claims are non-obvious over Nguyen et al in view of Lafon, Scammel, or Miller. Hence, the new claims have not been taught nor suggested by the references, alone or in combination, and as such are non-

obvious.

Claims 6-8, 22, 23, and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Rambert in view of Pitha. The Office Action alleges that Pitha teaches the use of 2-hydroxypropyl-β-cyclodextrin, and that one skilled in the art would find it obvious to prepare the Rambert compositions using a 50% 2-hydroxypropyl-β-cyclodextrin solution.

Applicants respectfully submit that Pitha does not cure the deficiencies of Rambert that were discussed previously, and hence the new claims are non-obvious over Rambert in view of Pitha.

Furthermore Applicants respectfully submit that the references, either alone, or in combination, do not teach the claimed invention. The instant claims involve the formation of inclusion complexes of a modafinil compound and a cyclodextrin such that modafinil has an aqueous solubility of at least 10 mg/ml, and wherein the molar ratio of cyclodextrin to modafinil is from about 10:1 to about 0.8:1. The Pitha reference presents a table of various drugs (other than modafinil) in hydroxypropyl- β-cyclodextrin solutions ranging from 40-50%. The data presented in Pitha is insufficient to determine the molar ratio of active agent to cyclodextrin. Hence, neither Nguyen, nor Pitha, nor either in combination, the teach the aqueous solubility of the instant invention, nor do they teach the molar ratios of the instant invention, and as such the newly amended claims are non-obvious.

In view of the above amendments and remarks, reconsideration and withdrawal of the rejections under §103 is respectfully requested.

Conclusion

In view of the above, it is believed that all the claims are in form for allowance, and

an early notification to that end is respectfully requested. Entry of the supplemental remarks and amendments and reconsideration of the present application is respectfully requested.

Respectfully submitted,

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